

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER: 20-816

CHEMISTRY REVIEW(S)

Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-816

REVIEW #1

DATE REVIEWED: 5/28/97

| <u>SUBMISSION TYPE</u> | <u>DOCUMENT DATE</u> | <u>CDER DATE</u> | <u>ASSIGNED DATE</u> |
|------------------------|----------------------|------------------|----------------------|
| SUBMISSION | 1/28/97 | 1/28/97 | 2/3/97 |
| AMENDMENT | 2/10/97 | 2/11/97 | 2/19/97 |
| AMENDMENT | 3/24/97 | 3/26/97 | 4/4/97 |

NAME & ADDRESS OF APPLICANT: Alcon Laboratories
Post Office Box 6600
Fort Worth, Texas 76115

DRUG PRODUCT NAME

Proprietary:

Azopt™

Established:

Brinzolamide

Code Name/#:

AL-4862; CAS 138890-62-7

Chem. Type/Ther. Class:

1S

PHARMACOL. CATEGORY:

glaucoma/elevated IOP

DOSAGE FORM:

Ophthalmic suspension

STRENGTHS:

1%

ROUTE OF ADMINISTRATION:

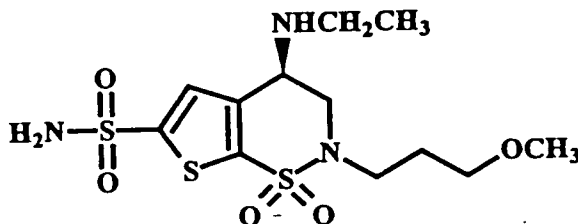
Topical ophthalmic

DISPENSED:

X Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

(R)-(+)-4-Ethylamino-2-(3-methoxypropyl)-3,4-dihydro-2H-thieno[3,2-e]-1,2-thiazine-6-sulfonamide-1,1-dioxide Molecular Formula: C₁₂H₂₁N₃O₅S₃ Molecular Weight: 383.49



REMARKS:

1. The drug substance is manufactured by two contract facilities. The information for is under Tab 1 in volume 3. That for is in the same volume under Tab 2.
2. The tradename has been sent on consult to the Labeling and Nomenclature Committee.
3. The EER is waiting for completion of the evaluation

CONCLUSIONS & RECOMMENDATIONS:

This application is **NOT APPROVABLE** due to some major deficiencies. Numerous lesser deficiencies were also found.

cc:

Orig. NDA 20-816

HFD-550/Division File

HFD-550/Chemist/Yaciw

HFD-550/CSO/Holmes

HFD-550/Medical/Ludwig

HFD-550/Pharm/Coulter

filename: N20816C1.REV

/S/

Charlotte A. Yaciw, Chemist, HFD-550/830

/S/ 8-6-97

Hasmukh Patel, Chemistry Team Leader HFD-550

Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-816

REVIEW # 2

DATE REVIEWED: 7/1/97

| <u>SUBMISSION TYPE</u> | <u>DOCUMENT DATE</u> | <u>CDER DATE</u> | <u>ASSIGNED DATE</u> |
|------------------------|----------------------|------------------|----------------------|
| SUBMISSION | 1/28/97 | 1/28/97 | 2/3/97 |
| AMENDMENT | 2/10/97 | 2/11/97 | 2/19/97 |
| AMENDMENT | 3/24/97 | 3/26/97 | 4/4/97 |
| AMENDMENT* | 6/24/97 | 6/25/97 | 6/30/97 |

*Submission covered in this review

NAME & ADDRESS OF APPLICANT: Alcon Laboratories
Post Office Box 6600
Fort Worth, Texas 76115

DRUG PRODUCT NAME

| | |
|--------------------------------|--------------------------|
| <u>Proprietary:</u> | Azopt TM |
| <u>Established:</u> | Brinzolamide |
| <u>Code Name/#:</u> | AL-4862; CAS 138890-62-7 |
| <u>Chem. Type/Ther. Class:</u> | 1S |

PHARMACOL. CATEGORY: glaucoma/elevated IOP

DOSAGE FORM: Ophthalmic suspension

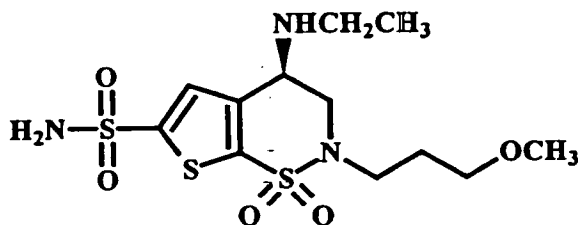
STRENGTHS: 1%

ROUTE OF ADMINISTRATION: Topical ophthalmic

DISPENSED: ☒ Rx ☐ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

(R)-(+)-4-Ethylamino-2-(3-methoxypropyl)-3,4-dihydro-2H-thieno[3,2-e]-1,2-thiazine-6-sulfonamide-1,1-dioxide Molecular Formula: C₁₂H₂₁N₃O₅S₃ Molecular Weight: 383.49



REMARKS:

1. This amendment contains updated stability data. Based on the data, this product may be assigned a 12 month expiration date. See the attached stability tables.
2. The tradename has been sent on consult to the Labeling and Nomenclature Committee. It is still pending as of this review.
3. The EER is waiting for completion of the evaluation . It is still pending as of this review.

CONCLUSIONS & RECOMMENDATIONS:

This application remains **NOT APPROVABLE** due to some major (and a number of minor) deficiencies documented in Review #1.

cc:

Orig. NDA 20-816
HFD-550/Division File
HFD-550/Chemist/Yaciw
HFD-550/CSO/Holmes
HFD-550/Medical/Ludwig
HFD-550/Pharm/Coulter

/s/
Charlotte A. Yaciw, Chemist, HFD-550/830

filename: N20816C2.REV

/s/ 8-6-97
Hasmukh Patel, Chemistry Team Leader HFD-550

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: August 5, 1997
FROM: Charlotte A. Yaciw, Chemist, HFD-550/830
TO: NDA 20-816
Through: Hasmukh Patel, CMC Team Leader, HFD-550
SUBJECT: EER and Tradename (Review #3)

The EER was found acceptable on July 15, 1997. A copy of the EES file is attached.

The Trademark Azopt was found acceptable on July 16, 1997. A copy of the response is attached.

These documents were received after the CMC Review #2 was completed (July 1, 1997).

This document is marked Review #3 for administrative purposes.

CC:
NDA 20-816
HFD-550/Division File
HFD-550/CMC/Yaciw
HFD-550/PM/LoBianco

Document ID:n20816c3.rev

Note:

*The microbiology staff
recommends approval of
this NOA. See attached
micro. review.*

HAB

REQUEST FOR TRADEMARK REVIEW

4/30/97
(818)

TO: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair, (HFD-530) CRP2

FROM: Division of Anti-inflammatory, Analgesic and Ophthalmic Products, HFD-550
Attention: Charlotte Yaciw Phone: 827-2511

DATE: April 8, 1997

SUBJECT: Request for Assessment of a Trademark for a Proposed Drug Product

Proposed Trademark: Azopt™

Company Name: Alcon

Established name, including dosage form: Brinzolamide ophthalmic suspension 1%

Other trademarks by the same firm for companion products:

Indications for Use (may be a summary if proposed statement is lengthy): "AZOPT™
Ophthalmic Suspension 1% is indicated in the treatment of elevated intraocular pressure in
patients with ocular hypertension or open-angle glaucoma." Brinzolamide is described as a
carbonic anhydrase inhibitor for ophthalmic use.

Initial comments from the submitter (concerns, observations, etc.):

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month.
Please submit this form at least one week ahead of the meeting. Responses will
be as timely as possible.

Rev Oct 96

Consult #818 (HFD-550) -

AZOPT

- brinzolamide ophthalmic suspension

The Committee found no look-alike/sound-alike conflicts or misleading aspects with the proposed proprietary name.

The Committee had no reason to find the proposed name unacceptable.

/s/ 7/16/97, Chair
CDER Labeling and Nomenclature Committee

**APPEARS THIS WAY
ON ORIGINAL**

FEB 1 1998

Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-816**REVIEW # 4****DATE REVIEWED:** 1/29/98

| <u>SUBMISSION TYPE</u> | <u>DOCUMENT DATE</u> | <u>CDER DATE</u> | <u>ASSIGNED DATE</u> |
|------------------------|----------------------|------------------|----------------------|
| SUBMISSION | 1/28/97 | 1/28/97 | 2/3/97 |
| AMENDMENT | 2/10/97 | 2/11/97 | 2/19/97 |
| AMENDMENT | 3/24/97 | 3/26/97 | 4/4/97 |
| AMENDMENT | 6/24/97 | 6/25/97 | 6/30/97 |
| AMENDMENT* | 12/15/97 | 12/16/97 | 12/19/97 |
| REVISED PKG INESRT* | 1/27/98 | | |
| AMENDMENT* | 1/28/98 | 1/29/98 | 1/29/98 |

*Submissions covered in this review

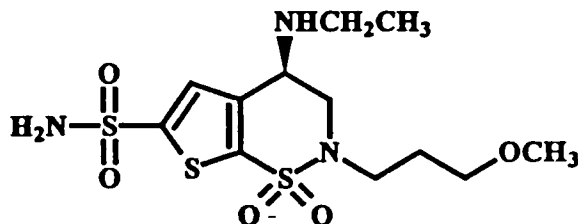
NAME & ADDRESS OF APPLICANT: Alcon Laboratories
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1. The 12/15/1997 amendment contains the responses to the issues listed in the 12/4/1997 Approvable letter. The 1/18/1998 amendment contains the proposed bottle and carton labeling in color.
2. Based on the data, this product may be assigned an 18 month expiration date except for the 2.5 mL fill size which should be limited to 12 months. See the attached updated stability summary.
3. The trade name, Azopt, was found acceptable by the Labeling and Nomenclature Committee on July 16, 1997.
4. The EER was found acceptable on July 15, 1997.
5. The methods validation is pending (see attached E-mail).

CONCLUSIONS & RECOMMENDATIONS:

CC:

HFD-550/Pharm/Coulter

151

Hasmukh Patel, Chemistry Team Leader HFD-550

15

2-1-98

**APPEARS THIS WAY
ON ORIGINAL**